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Mertz, Kenneth H.; Reitelseder, Soren; Jensen, Mikkel; Lindberg, Jonas; Hjulmand, Morten; Schucany, Aide; Andersen, Soren Binder; Bechshoeft, Rasmus L.; Jakobsen, Markus D.; Bieler, Theresa; Beyer, Nina; Nielsen, Jakob Lindberg; Aagaard, Per; Holm, Lars

Published in:
Scandinavian Journal of Medicine & Science in Sports

DOI:
10.1111/sms.13524

Publication date:
2019

Document version
Peer reviewed version

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Article type   : Original Article

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Running title: Asymmetry and function in older adults

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/sms.13524

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ACKNOWLEDGEMENTS

Author contributions: SR, RB, NB, TB, PA, and LH designed the study. MJ, JL, MH, AS and SA collected the data. KM collected the data and drafted the manuscript. JLN and MDJ helped with data analysis. All authors contributed to the revision of the manuscript. This work was supported by the University of Copenhagen Excellence Programme for Interdisciplinary Research, Arla Foods Ingredients Group P/S and the Danish Dairy Research Foundation.

ABSTRACT

Purpose: Numerous daily tasks such as walking and rising from a chair involve bilateral lower limb movements. During such tasks lower extremity function (LEF) may be compromised among older adults. LEF may be further impaired due to high degrees of between-limb asymmetry. The present study investigated the prevalence of between-limb asymmetry in muscle mass, strength and power in a cohort of healthy older adults, and examined the influence of between-limb asymmetry on LEF.

Methods: 208 healthy older adults (mean age 70.2±3.9 years) were tested for LEF (400 m walking and 30-s chair stand). Furthermore, maximal isometric and dynamic knee extensor strength, leg extensor power, and lower limb lean tissue mass (LTM) were obtained unilaterally.

Results: Mean between-limb asymmetry in maximal muscle strength and power ranged between 10-13%, whereas LTM asymmetry was 3±2.3%. Asymmetry in dynamic knee extensor strength was larger for women compared to men (15.0±11.8% vs 11.1±9.5%; P=0.005) Leg strength and power were positively correlated with LEF (r^2=0.43-0.46, P<0.001). The weakest leg was not a stronger predictor of LEF than the strongest leg. Between-limb asymmetry in LTM and isometric strength were negatively associated with LEF (LTM; r^2=0.12, P=0.005, isometric peak torque; r^2 =0.40, P=0.03.) but dynamic strength and power were not.

Conclusion: The present study supports the notion that in order to improve or maintain LEF, healthy older adults should participate in training interventions that increase muscle strength and power, whereas the effects of reducing between-limb asymmetry in these parameters might be of less importance.

Keywords: lower extremity function, mobility, muscle strength, muscle power, asymmetry

INTRODUCTION

Age-related loss of muscle mass, which has been to reported begin around the 5th decade of life[1,2],can be responsible for an increased risk of metabolic disorders, functional impairment and frailty[1,3]. While muscle mass is progressively lost by ~0.5% annually[4], the accompanying impairments in muscle strength and power are observed to occur at a faster rate of up to 3-4% annually[5–7]. Impairment in these factors has been shown to be a strong predictor of current functional capacity[8,9] as well as being associated with an elevated risk of developing future functional limitations[6,10]. However, in well-functioning older individuals the initial loss of muscle strength and power may not have strong impact on functional capacity, as the relationship between muscle strength/power and functional capability appears to be plateauing (i.e. reach a ceiling region) at the upper end of this relationship[11].

A vast number of physical activities of daily living (ADL) involve bilateral lower limb movements (walking, chair stand, stair climbing, etc.), and the ability to perform these activities will therefore be limited by bilateral lower limb muscle function. Thus, another possible determinant of functional capacity could be the degree of lower limb asymmetry in the aforementioned factors. Previous studies have observed that high between-limb asymmetry in leg extensor power is associated with impaired postural balance and an elevated incidence of falls[12,13]. These findings suggest that between-limb differences (asymmetry) in lower limb muscle size, strength and/or power can negatively ADL in old adults. Thus, the magnitude of between-limb asymmetry in lower limb muscle function may represent a separate and early detectable risk factor for impaired functional capacity even in healthy non-frail older adults. This hypothesis has only been sparsely investigated with inconclusive results[14–16]. The discrepancy between observations could potentially be due to differences in testing methods (testing of whole-leg vs. single-joint power), as well as lack of statistical adjustments for physical activity and levels of body fat[17]. Therefore, research using both whole-leg and single-joint testing methods to investigate the potential influence of between-limb asymmetry on functional capacity in older adults is warranted. Furthermore, as the risk of functional impairment seems to be higher in women compared to men[18–20], investigations of sex specific differences in lower extremity asymmetry are of key interest.

The aim of this study, therefore, was to quantify the magnitude of between-limb asymmetry in lower limb skeletal muscle mass, strength and power in a large cohort of healthy home-dwelling Danish older men and women. Secondly, we aimed to investigate to which extent lower extremity function (LEF) would be determined (i.e regressionally predicted) by selected measures of muscle mass, strength and power, and/or by the degree of between-limb asymmetry in these parameters.

MATERIAL & METHODS

This study was based on cross-sectional analyses of baseline data obtained in the Copenhagen CALM study[21]. A full description of the CALM protocol, as well as detailed exclusion criteria have been presented elsewhere[21]. A brief description of the experimental methods is provided below.

Participants

A total of 208 home-dwelling older adults with a mean age of 70 ± 4 (SD) years were recruited for the study (Women: 99, Men: 109). All participants gave their written consent in accordance with the declaration of Helsinki II, and the study was approved by the Danish Regional Ethics Committees of the Capital Region (H-4-2013-070). Anthropometric data of the included participants are listed in Table 1. Recruitment was conducted via advertisements in newspapers, magazines, and social media, as well as presentations at senior centers and public events. To be included in the study, participants were not allowed to participate in more than 1 hour of heavy resistance training per week, but were allowed to perform other forms of exercise. Participants were excluded if they possessed any medical condition potentially preventing them from safely completing a 1-year intervention including heavy resistance training and twice daily protein/carbohydrate supplementation. A full description of exclusion criteria can be found elsewhere[21].

Physical performance assessment

All physical performance tests were carried out by an experienced assessor on the same day in the order listed below. Measurement of body composition was done on a separate day. The entire test battery was typically completed within 1 hour, and rest periods between tests were administered as needed. Participants arrived to the Lab in clothes and shoes intended for physical activity. Prior to the test day participants had been carefully instructed not to perform any strenuous physical activities 2 days prior to the performance tests. Prior to the tests, the dominant leg of the participants was determined by asking them which leg they felt was the strongest.

Lower extremity function

The 400 m walk test and the 30-s chair stand test were chosen as objective measures of LEF[22,23].

The 400 m walk test was performed on a 20-m indoor course track marked by two colored cones. The participants were instructed to walk 400 m as fast as possible without running and without receiving personal assistance or sitting down during the test[22,24]. Data was reported as time to complete 400 m walk. For the later calculation of the composite LEF measure, walk time was converted into average walking speed as this parameter has been shown to be a strong predictor of mobility limitations in older adults[24].

The 30-s chair stand test was performed using a chair without armrest (seat height 44.5 cm). Participants completed as many sit-to-stands as possible in 30 s with their hands crossed over the chest. A repetition was defined as the participant rising from a seated position to reach full extension of the knees and hips. This test has previously been shown to be a valid and reproducible test of functional lower body strength in older adults[23].

The composite sum of the Z-scores of each of the two test parameters (average 400 m walk speed and number of stands in the 30-s chair test) was calculated to provide a global index for LEF, which was used in the subsequent statistical analyses[16,25].

Maximal leg extensor power

Unilateral leg extensor power (LEP) was measured using the Nottingham power rig (Queens Medical Center, Nottingham University, UK) as described in detail elsewhere[12,26]. In brief, participants were seated with their hands folded over the chest, and carefully instructed to press a pedal down as hard and fast as possible by extending the knee and hip joint, thereby accelerating a flywheel. Based on the rotational speed of the flywheel, a computer calculated the average power exerted in each single leg extension movement. The participants were familiarized to the procedure by performing two submaximal warm-up trials, followed by a minimum of five maximal trials each separated by 30 s of rest. The test ended when participants performed two consecutive results that were lower than their current peak average power value. The self-reported dominant leg was tested first, followed by the self-reported non-dominant leg.

Maximal knee extensor strength

Maximal concentric knee extensor strength (gravity corrected peak torque) was measured during slow (60°/s) maximal knee extension using an isokinetic dynamometer (Kinetic Communicator, model 500-11, Chattanooga, TN, USA) at a knee joint range of motion from 90° to 10° knee flexion (0° = full knee extension). Following three warm-up trials at submaximal effort, participants performed a minimum of 4 maximal knee extension trials with strong verbal encouragement and visual online display of the exerted torque, separated by 30-45 s of rest. Subsequently, trials were repeated until participants were unable to improve knee extensor peak torque any further. The self-reported dominant leg was tested first, followed by the non-dominant leg. For each leg the trial with the highest gravity-corrected peak torque (calculated by multiplying the gravity-corrected dynamometer force by the length of the dynamometer lever arm) was selected for further analysis.

Finally, participants performed three maximal isometric knee extensor contractions (MVIC) at 70° knee flexion separated by 30-45 s rest. Participants were instructed to contract as hard and fast as possible with strong verbal encouragement for approximately 4 s. The trial with the highest peak torque was selected for further analysis. Attempts containing an initial countermovement were disqualified, and a new trial was performed.

Body composition

Body composition was assessed using dual-energy X-ray absorptiometry (Lunar iDXA, GE Medical Systems, Pewaukee, WI, USA). Study participants refrained from strenuous activities for 48 hours prior to the test. They arrived fasting from 21:00 the night before, but were allowed to drink water as needed prior to the scansand. All scans were performed between 08:00 and 10:00. From these scans lean tissue mass (LTM) were obtained for the left and right lower limbs (Segmented at the femoral neck). Using these measures, appendicular skeletal muscle mass index (ASMI) was calculated as previously described[27] by dividing the sum of LTM (subtracted by fat and bone mineral content) of arms and legs by height squared. Body fat percentage and visceral fat content were also assessed. Regions of interest (ROIs) for the extremities and visceral body parts were set based on the defaults definitions provided by the scanner software. The same examiner controlled the default positioning of all regions, which were adjusted slightly when appropriate.

Activity monitoring

Daily activity levels were measured by mounting an accelerometer-based activity monitor (activPal 3™, activPal 3c™, or activPal micro; PAL technologies, Glasgow, UK) on the anterior surface of the thigh[28]. The activity monitor was worn for 96 continuous hours covering two weekdays and a full weekend. Data was reported as the average number of steps per day.

Statistical analysis

Group characteristics were compared using unpaired t-tests or Wilcoxon rank-sum tests for Gaussian and non-Gaussian distributed data, respectively. Unilateral strength and LTM for the strongest and weakest leg were analyzed using multiple linear regression with sex, strongest/weakest limb and age as independent variables. Relationships between dependent variables (Composite Z-score) and independent variables (various muscle mechanical parameters) including co-variables (sex, age, steps per day, fat percentage, and BMI) were performed using multiple linear regression analysis. Steps per day were used to control for daily activity levels, whereas the assessment of body fat was used to account for potential effects of differences in body composition. These specific co-variables were selected as they have previously been shown to affect LEF[17,20] Co-variables with low weight in the model ($P>0.1$) were excluded using progressive step-wise regression. Robust standard errors were calculated when linear regression models showed heteroscedasticity. Percentage between-limb asymmetry was calculated as (([Strongest – Weakest]/Strongest)*100).

Between sex comparisons for limb asymmetry were performed using Wilcoxon rank-sum tests (assuming non-Gaussian distributions). Results are reported as mean ± SD unless otherwise stated, and the level of significance was $P < 0.05$ (2-tailed testing). All statistical analyses were performed using STATA 15.1 (StataCorp, TX, USA).

RESULTS

Characteristics of research participants

Table 1 presents the characteristics of the included participants. Compared to female participants, male participants demonstrated higher ($P < 0.0001$) ASMI, lower body fat percentage, higher visceral fat content, and tended to have higher BMI ($P = 0.07$). Furthermore, male participants demonstrated faster 400 m gait speeds ($P = 0.0001$) and completed more repetitions on the 30-s chair stand test ($P = 0.001$). No sex differences were observed for age or daily activity level.

Muscle strength and mass

Data on maximal unilateral muscle strength and power, as well as muscle mass were grouped into the strongest and weakest limb (Presented in Table 2). Male participants exhibited greater LEP, dynamic knee extensor strength, and MVIC (all normalized to body mass) compared to female participants, along with larger leg LTM (all $P < 0.001$).

Between-limb asymmetry

Data on between-limb asymmetry are presented in Figure 1. The average between-limb asymmetry ranged between 10-13% for various strength and power measurements (LEP: 10.6 ± 7.9%; Dynamic peak torque: 13.0 ± 10.8%; MVIC: 11.2 ± 10.3%), whereas asymmetry in leg LTM averaged 3.0 ± 2.3%. Asymmetry was larger in women compared to men for dynamic peak torque (Men 11.1 ± 9.5%; Women: 15.0 ± 11.8%; $P = 0.005$). For all other measures, asymmetry did not differ between sexes.

Associations between strength, power and asymmetry and lower extremity function (LEF)

LEF was positively correlated with LEP, MVIC, and dynamic peak torque (r^2 = 0.43-0.47, P < 0.001) (Table 3). In addition, leg LTM was positively correlated with LEF (r^2 = 0.38, P = 0.02-0.03). Leg LTM was not associated with LEF using the non-adjusted regression model. Associations to LEF were comparable when correlating strength or power levels from either the strongest or weakest leg.

Percentage between-limb asymmetry in MVIC was negatively associated with LEF when adjusted for steps per day and body fat percentage (r^2 = 0.40, P = 0.025). Likewise, leg LTM asymmetry was negatively correlated with LEF when adjusted for steps per day, although demonstrating a weaker relationship (r^2 = 0.12, P = 0.048). These associations disappeared when using non-adjusted regression analysis. Percentage between-limb asymmetry in LEP and dynamic peak torque were not associated with LEF.

DISCUSSION

The present study evaluated the degree of between-limb asymmetry in maximal leg muscle strength, power, and lower limb LTM in order to investigate its potential association with functional capacity among home dwelling older individuals.

The data revealed that the mean magnitude of lower limb muscle strength and power asymmetry was in the range of 10-13%, whereas asymmetry in leg LTM was much lower (3%). At group level the magnitude of between-limb asymmetry was comparable to values previously reported in healthy older adults of similar age[13,14,16,29]. Notably however, a significant proportion (11-20%) of the participants demonstrated much greater (2-3 fold higher) levels of between-limb asymmetry in lower limb strength and power, which might predispose this subpopulation for future mobility limitations. Surprisingly, women demonstrated higher degrees of between-limb asymmetry in dynamic knee extensor peak torque than men. To our best knowledge, this effect of sex on between-limb asymmetry has not been reported previously. This finding could, at least in part, help to explain previous observations of lower LEF and higher risk of developing frailty in older women compared to men[18,30]. However, since sex differences were not apparent for any other outcome measure obtained in the present study, this notion remains purely speculative.

The present study demonstrated moderate-to-strong associations between maximal leg extensor strength/power and LEF (Table 3). Comparable relationships have been observed in previous studies[14,15,31] although these studies generally were performed in elderly with lower functional performance levels than the older adults examined in the present study. For instance, 90% of the participants in the present study completed the 400 m walk in a time that would place them in the fastest quartile reported by Newman and coworkers[24]. Importantly, the present associations suggest that even in healthy independently living and active older individuals, high levels of leg muscle strength and/or power are accompanied by high LEF and vice versa. Some measures of LEF seem to suffer from a ceiling effect when applied in healthy older adults[32], underlining the importance of choosing sufficiently challenging tests when measuring LEF in this population. In contrast to previous reports[31,33–35] we did not find LEP to be a stronger predictor of functional performance than isolated muscle strength parameters (dynamic or isometric knee extensor strength). It is possible that this apparent discrepancy arise as a result of the overall high strength and functional performance level of the present group of old adults.

Leg LTM as a measure of lower limb muscle mass appeared to be a moderate predictor of LEF in our cohort when adjusted for age, daily activity level, and body fat percentage. In contrast, leg LTM failed to predict LEF when using a non-adjusted linear regression model. Previous investigations into the relationship between muscle mass and functional performance levels in older adults have shown conflicting results, with some studies reporting positive correlations[1,27,36] while absent in others[9,37–39]. Importantly, leg LTM failed to predict LEF when using a non-adjusted linear regression model. However, a clear positive relationship between leg LTM and LEF emerged when the effects of age, physical activity and body fat percentage were accounted for. In turn, the observed association between muscle mass (leg LTM) and lower extremity function may have been mainly driven by the positive relationships between lower limb strength and/or power levels and LTM. This can be considered an independent benefit of conserving muscle mass at old age regardless of other potential advantages hereof on metabolic health, systemic inflammatory state etc[40].

The present study revealed that when using an adjusted regression model, high levels of between-limb asymmetry in MVIC and leg LTM were associated with reduced LEF even when examined in well-functioning community-dwelling healthy older adults. In contrast, the degree of lower-limb asymmetry in LEP and dynamic peak torque failed to demonstrate any associations with LEF. These disparate trends are puzzling, as asymmetry in these measures would be expected to depend largely on the same physiological factors, and consequently should be similarly associated to LEF. Although speculative, the disparate trends could possibly be due to asymmetry in MVIC being dependent on differences in maximal force generation capacity of the lower limbs, and thus largely rely on skeletal muscle mass (size). In contrast, asymmetry in LEP and dynamic peak torque might to a greater extent depend on between-limb differences in neuromuscular activation and coordination due to the highly dynamic nature of the tests, which involved slow isokinetic to fast non-restricted movement speeds. Further, we intended to examine whether LEF were influenced directly by the strength/power performances of the strongest or weakest leg, respectively. Somewhat unexpectedly, however, neither the prevalence nor strength of associations to functional performance differed between the strongest or weakest limbs, suggesting that the strength/power capacity of the weakest leg generally does not represent a separate limiting factor for lower extremity function, at least in healthy older individuals. Thus, in terms of lower limb muscle strength and power the present findings suggest the existence of a substantial physical reserve among healthy older individuals, whereby lower single-limb strength/power levels (and/or potential inter-limb asymmetries herein) may remain beyond any critical threshold below which it would start to negatively affect physical function[11]. Supporting the present observations, LaRoche and colleagues[14] also reported the weakest leg to not be a better predictor of functional performance than the stronger leg in community dwelling older adults at risk of mobility limitation.

Methodological considerations: Potential limitations may be observed with the present study. A low degree of between-limb asymmetry was observed in the lower limbs LTM (~3%). Given the inherent limitations of DXA scanning to detect subtle differences in lean segment mass[41], future studies investigating between-limb asymmetry in healthy older adults would benefit from using more sensitive techniques such as magnetic resonance imaging or CT.[42]Furthermore, it would have been relevant to include measurements of postural balance , since elevated between-limb asymmetry in LEP has previously been observed in fallers compared to non-fallers[13], although not consistently observed in all studies[29]. Also, given the cross-sectional nature of the present study, no direct causalities could be revealed from the present observations. Longitudinal follow-up on the long-term development in functional capabilities would, therefore, be of strong interest.

In summary, between-limb asymmetry in maximal lower limb muscle strength and power production showed no systematic associations to LEF in a cohort of 208 healthy independently living and active adults aged 65 years and above. Yet, a number of lower limb strength (MVIC) and power (LEP) parameters were moderately-to-strongly associated with LEF.

Perspective: The present observations support previous notions that strength training intervention should be introduced in healthy older adults in order to preserve or even better increase maximal muscle strength and power[43,44], whereas the potential benefits from reducing between-limb asymmetry in selected muscle strength/power or muscle mass parameters seems to remain of lesser importance. Future studies should investigate how specific types of unilateral and bilateral strength/power training will affect lower limb muscle mass, strength and power of well-functioning older adults, while concurrently assessing to which extent these changes can be translated into improvements in functional capacity.

CONFLICT OF INTEREST

None to report.

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Table 1. Characteristics of the research participants.

		All			Men			Women			P-value
N =		208			109			99			-
Age	**[y]**	70.2	±	3.9	70	±	3.9	70.4	±	3.9	0.52
Weight	[kg]	75.7	±	12.8	81.4	±	11.2	69.4	±	11.4	<0.0001
Height	[m]	1.72	±	0.08	1.77	±	0.06	1.67	±	0.06	<0.0001
BMI	[kg/m^2]	25.6	±	3.8	26.0	±	3.4	25.1	±	4.1	0.07
ASMI	[kg/m^2]	7.6	±	1.2	8.3	±	0.9	6.7	±	0.8	<0.0001
Fat%	[%]	33.3	±	8.1	29.0	±	6.4	37.9	±	7.2	<0.0001
Visceral fat	[kg]	1.3	±	0.9	1.7	±	0.9	0.9	±	0.7	<0.0001
400 m gait time	[s]	245	±	34	236	±	32	255	±	33	0.0001
30 s chair stands	[reps]	19.7	±	5.0	20.7	±	4.8	18.6	±	5.0	0.001
Daily stepcount	[steps]	10056	±	3958	10040	±	3877	10163	±	4099	0.83

Results are reported as mean ± SD. P-values derived using unpaired t-testing or Wilcoxon rank-sum comparison between sexes. BMI = Body mass index; ASMI = Appendicular skeletal muscle index.

Table 2. Unilateral knee extensor strength, leg extensor power and fat-free mass (LTM).

			Strongest limb	Weakest limb	Gender effect
Leg extensor power	[W/kg]	All	2.63 ± 0.68	2.32 ± 0.63	
		Men	3.00 ± 0.63	2.65 ± 0.60	< 0.001
		Women	2.23 ± 0.48	1.97 ± 0.47	
Dynamic peak torque	[Nm/kg]	All,	2.04 ± 0.45	1.78 ± 0.46	< 0.001
		Men	2.27 ± 0.39	2.02 ± 0.40	
		Women	1.78 ± 0.38	1.51 ± 0.39	
MVIC	[Nm/kg]	All,	2.29 ± 0.54	2.04 ± 0.54	< 0.001
		Men	2.55 ± 0.47	2.30 ± 0.45	
		Women	2.01 ± 0.46	1.76 ± 0.49	
LTM legs	[kg]	All,	8.66 ± 1.68	8.41 ± 1.66	< 0.001
		Men	9.88 ± 1.20	9.59 ± 1.21	
		Women	7.31 ± 0.94	7.09 ± 0.94	

Notes: Results are reported as mean ± SD. Data on knee extensor dynamic peak torque, isometric peak torque (MVIC), and leg extensor power are reported normalized to body weight. Lean tissue mass (LTM) measures are reported in absolute values. P-values represent the outcome of linear regression analyses.

Table 3. Relationships between Lower extremity function (LEF) and lower body strength-/power or fat free mass (LTM) of the strongest or weakest leg, or between-limb asymmetry (%ASYM).

Associations to LEF		Included covariables					P-value	R^2
		Gender	Age	Steps/day	Fat-%	BMI		
Leg extensor power	*Strongest leg*	**	**	*	***	-	<0.001	0.44
	Weakest leg	**	**	**	***	-	<0.001	0.45
	%ASYM	-	-	-	-	-	0.36	0.004
Dynamic peak torque	*Strongest leg*	***	*	**	***	-	<0.001	0.47
	Weakest leg	**	**	**	***	-	<0.001	0.45
	%ASYM	-	-	-	-	-	0.07	0.02
MVIC	*Strongest leg*	**	**	**	***	-	<0.001	0.46
	Weakest leg	**	**	**	***	-	<0.001	0.47
	%ASYM	-	***	*	***	-	0.03	0.40
Leg LTM	*Strongest leg*	-	***	*	***	-	0.02	0.38
	Weakest leg	-	***	*	***	-	0.03	0.38
	%ASYM	-	-	***	-	-	0.005	0.12

Notes: “P-value” indicates the level of significance for the correlation. Levels of significance for covariables are shown as: * P<0.1, ** P<0.01, *** P<0.001. “-“ P>0.1.

LEGENDS

Figure 1. Percentage between-limb asymmetry in power, strength, and muscle mass measures. Asymmetry was calculated as (((Strongest – Weakest)/Strongest)*100%). Results are shown as mean ± SD. * denotes significant difference between sexes ($P < 0.05$). MVIC; Maximal voluntary isometric contraction. Leg LTM; Leg lean tissue mass.